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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,476	12/07/2001	Norbert O. Reich	G&C 30794.30-US-D1	8266

7590 09/22/2005

Attn: Karen S. Canady
Gates & Cooper LLP
Howard Hughes Center
6701 Center Drive West, Suite 1050
Los Angeles, CA 90045

EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/010,476

Applicant(s)

REICH ET AL.

Examiner

Traviss C. McIntosh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-27 and 32-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-27 and 32-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

It is noted that applicants were not required to reply to the office action mailed out on March 29, 2005, as the examiner is sending out this office action to replace that one per the interview summary mailed on April 20, 2005. As such, this office action is being sent based on the RCE filed on January 10, 2005 and the claims filed on November 9, 2004.

Claims 1-20 and 28-31 are canceled.

Claims 36-39 have been added.

An action on the merits of claims 21-27 and 32-39 is contained herein below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

In the instant application, independent claim 21 is drawn to a method of inhibiting DNA methylation by contacting DCMTase with a synthetic inhibitor molecule which comprises a C-5

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methylcytosine. Dependent claims 36-39 provide that the synthetic inhibitor molecule of claim 21 comprises an oligonucleotide having a nucleotide sequence of either SEQ ID NO: 10, 13, 14, or 15. It is noted that the examiner believes that applicants intend the methylcytosine molecule to be included in the sequences filed, as evidenced by applicant's figures. See figure 1B for example, where SEQ ID 15 is shown to be 5'TTGCCC^{be}mCGCCCCTT3'. The monomer represented by mC is intended to the methylcytosine moiety. However, the sequence listings filed by applicants do not include said methylcytosine monomer in the sequences. The examiner does not believe applicants were in possession of all of the sequences as filed in the sequence listings, as the invention is drawn to using C-5 methylcytosine containing molecules, which the sequences as filed are not seen to contain.

SDW
9/17/05

Claim Rejections - 35 USC § 102

Applicant's arguments, in amendment filed 11/9/04, with respect to the rejection(s) of claim(s) 21-27 and 32-35 under 35 USC 102(b) have been fully considered and are persuasive. Specifically, applicants arguing that the method of Sufrin et al. was not practiced in the presence of DNA. Therefore, the rejection has been withdrawn. However, upon further consideration, a new obviousness type rejection is made in view the same reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 24, and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sufrin et al. (US Patent 5,652,105).

Claim 21 is drawn to a method of inhibiting the methylation of DNA comprising contacting a DCMTase with a synthetic inhibitor molecule in the presence of DNA wherein the inhibitor molecule comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 24 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule. Claim 33 provides that the

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subject is human, claim 34 provides the subject is an animal, and claim 35 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61).

What is not taught specifically is method being practiced in the presence of DNA nor the binding to an allosteric site on the DCMTase.

It is noted that these claims were previously rejected under 35 USC 102 as being anticipated, but since the prior art does not specifically teach binding in the presence of DNA, the claims are not seen to be anticipated.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Sufrin et al. in the presence of DNA. Moreover, it is noted that the step of "binding to an allosteric site" is seen to be inherently taught by Sufrin et al. as the binding of the compound to an allosteric site must have occurred in Sufrin et al. as this is a direct result of the compounds properties. That is, the instant application and Sufrin et al. both contact a 5-methylcytosine DNA with DCMTase wherein DCMTase activity was subsequently inhibited, thus the binding to an allosteric site must have inherently been performed in Sufrin et

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al. Additionally, it is noted that Sufrin et al. teach their substrates to be DNA analogs comprising from 12-50 nucleobases in length (column 3, lines 4-23). Moreover, Sufrin et al. state that their analogs are specifically ascribed to their effects on DCMTase and therefore the process of DNA methylation in cells (column 3, lines 25-28). Thus, Sufrin et al. clearly suggest the use of their 5-methylcytosine containing DNA's to be used to inhibit DCMTase and thus inhibit the process of DNA methylation in cells. Moreover, Sufrin et al. state that their DNAs could be useful in treating cancers, since inhibition of DNA methylation has been shown to cause differentiation of certain types of tumor cells (column 7, lines 65-68). Thus, Sufrin et al. are clearly intending their method to be practiced in the presence of DNA, as it is well known in the art that DCMTase methylates DNA, and thus inhibiting DCMTase with their DNAs would inhibit DNA methylation.

Claims 22-23, 25-27, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sufrin et al. (US Patent 5,652,105).

Claim 22 is drawn to a method of inhibiting the proliferation of cancer cells comprising administering a synthetic inhibitor molecule that comprises a C-5 methylcytosine molecule which binds to an allosteric site on the DCMTase, which inhibits the methyltransferase activity. Claim 23 provides that the cancer is from lung, breast, prostate, pancreas, or colon. Claim 25 provides that the subject is human, claim 26 provides the subject is an animal, and claim 27 provides the animal is porcine, piscine, avian, feline, equine, bovine, ovine, caprine, or canine.

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Claim 32 provides that the inhibitor is an oligonucleotide comprising the C-5 methylcytosine molecule.

Sufrin et al. disclose an oligomeric DNA analog which comprises at least one 5-methylcytosine residue which specifically interacts with mammalian DCMTase (abstract). Moreover, Sufrin et al. disclose that their analogs are useful to inhibit DNA methyltransferase activity in tumor cells (column 3, lines 28-33). Sufrin et al. additionally disclose that their analogs appear to interact with both an activation and a catalytic site on the enzyme (column 7, lines 29-31). Moreover, Sufrin et al. disclose that their analogs were artificially constructed (column 4, lines 54-58). Sufrin et al. disclose that their analogs are effective in inhibiting DCMTase activity in humans (column 1, lines 42-53) as well as mice (column 2, lines 52-61). Moreover, Sufrin disclose that lowering the level and activity of DCMTase also lowers the incidence of colon cancer (column 2, lines 52-61).

What is not taught specifically is method being practiced in the presence of DNA nor the binding to an allosteric site on the DCMTase.

It is noted that these claims were previously rejected under 35 USC 102 as being anticipated, but since the prior art does not specifically teach binding in the presence of DNA, the claims are not seen to be anticipated.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Sufrin et al. in the presence of DNA. Moreover, it is noted that the step of "binding to an allosteric site" is seen to be inherently taught by Sufrin et al. as the binding of the compound to an allosteric site must have occurred in Sufrin et al. as this is a direct result of the compounds properties. That is, the instant application and Sufrin et al. both

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contact a 5-methylcytosine DNA with DCMTase wherein DCMTase activity was subsequently inhibited, thus the binding to an allosteric site must have inherently been performed in Sufrin et al. Additionally, it is noted that Sufrin et al. teach their substrates to be DNA analogs comprising from 12-50 nucleobases in length (column 3, lines 4-23). Moreover, Sufrin et al. state that their analogs are specifically ascribed to their effects on DCMTase and therefore the process of DNA methylation in cells (column 3, lines 25-28). Thus, Sufrin et al. clearly suggest the use of their 5-methylcytosine containing DNA's to be used to inhibit DCMTase and thus inhibit the process of DNA methylation in cells. Moreover, Sufrin et al. state that their DNAs could be useful in treating cancers, since inhibition of DNA methylation has been shown to cause differentiation of certain types of tumor cells (column 7, lines 65-68). Thus, Sufrin et al. are clearly intending their method to be practiced in the presence of DNA, as it is well known in the art that DCMTase methylates DNA, and thus inhibiting DCMTase with their DNAs would inhibit DNA methylation.

The invention of claims 21-27 and 32-35 is seen to be prima facie obvious in view of the Sufrin et al. reference.

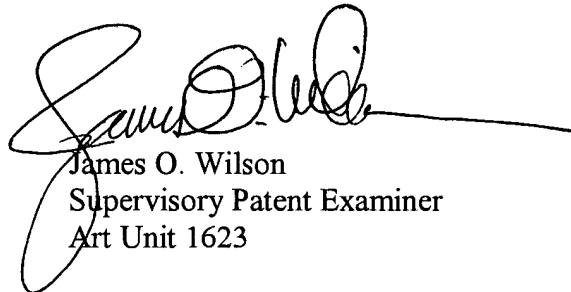
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh III
September 15, 2005



James O. Wilson
Supervisory Patent Examiner
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